

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Seiichi Araki et al.  
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Entitled: A MEDICAMENT CONTAINING A RIBOFLAVIN COMPOUND  
Examiner: A. R. Hughes  
Art Unit: 1614

MAIL STOP AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

DECLARATION OF DR. KOHTARO KODAMA UNDER 37 C.F.R. § 1.132

I, Dr. Kohtaro Kodama, declare as follows:

1. I have received a Bachelor of Pharmacology from Kyushyu University, Fukuoka in Japan in 1988, and a Doctor of Pharmacology in 1999 from the same institution.
2. I have been engaged in research and study of pharmacology of the cardiovascular, urinary, emergency medical care and gastrointestinal systems at Tsukuba Research Laboratories in Eisai Co., Ltd. from April 1990 until March 2007. Currently, I am a researcher in the field of pharmacology of the cardiovascular system at Eisai Co., Ltd.
3. In work conducted at Tsukuba Research Laboratories, EISAI CO., LTD., 1-3, Tokodai 5-chome, Tsukuba-shi, Ibaraki 300-2635, Japan under my direction and supervision, we tested the effect of vitamin B2 (riboflavin sodium phosphate) on glutathione levels in erythrocytes from mice and rats.
4. LPS (lipopolysaccharide) was intravenously injected into male ICR (The Institute for Cancer Research) mice or SD (Sprague-Dawley) rats. Vitamin B2 at 20 mg/kg or vehicle was intravenously administered 1 hour after LPS injection.

5. Whole blood was collected 6 hours after LPS injection. The collected whole blood was centrifuged and deproteinated erythrocytes were used for the glutathione assay by using glutathione assay kit (CAYMAN: Ann Arbor, MI, USA). Each value is expressed as the mean of 2 data.

6. The findings are illustrated in the table below:

Glutathione levels in erythrocytes were not changed both in rats and mice.

Glutathione ( $\mu$ M)		
	Rat	Mouse
Vehicle	19.4	18.6
LPS	19.4	17.4
LPS+Vitamin B2	20.3	15.8

7. The data presented herein indicate that vitamin B2 had no effect on glutathione levels in erythrocytes in LPS-treated rats and mice.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above application and any patent or application related thereto.

Kohtaro Kodama  
Dr. Kohtaro Kodama

Oct. 2, 2008  
Date